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Diet and Nutrient Intakes and Risk of Non-Hodgkin's Lymphoma in Connecticut Women

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A population-based case-control study (601 cases and 717 controls) was conducted in 1995–2001 among Connecticut women to evaluate the relation between diet and nutrient intakes and the risk of non-Hodgkin's lymphoma (NHL). When the highest quartile of intake was compared with the lowest, the authors found an increased risk of NHL associated with animal protein (odds ratio = 1.7, 95% confidence interval: 1.2, 2.4) and saturated fat (odds ratio = 1.9, 95% confidence interval: 1.1, 2.3) but a reduced risk for polyunsaturated fat (odds ratio = 0.6, 95% confidence interval: 0.4, 0.9) and no relation for vegetable protein and monounsaturated fat. An increased risk was also observed for higher intakes of retinol, eggs, and dairy products. On the other hand, a reduced risk was found for higher intakes of dietary fiber and for several fruit and vegetable items. Risk of NHL associated with diet and nutrient intakes appeared to vary based on NHL subtype. An association between dietary intake and NHL risk is biologically plausible because diets high in protein and fat may lead to altered immunocompetence, resulting in an increased risk of NHL. The antioxidant or inhibiting nitrosation reaction properties of vegetables and fruits may result in a reduced risk. Further investigation of the role of dietary intakes on the risk of NHL is warranted.

case-control studies; diet; dietary fats; lymphoma, non-Hodgkin; proteins; risk factors; women

Abbreviations: CI, confidence interval; NHL, non-Hodgkin's lymphoma; OR, odds ratio; RR, relative risk.

The incidence and mortality rates of non-Hodgkin's lymphoma (NHL) have been increasing in many parts of the world (1). In the United States, the incidence of NHL has risen faster than the incidence of all other cancer types except melanoma and female lung cancer (1). Studies from the Connecticut Tumor Registry showed no indication of a decline or plateau in incidence rates among recent birth cohorts, suggesting that the incidence rate of NHL in Connecticut is likely to continue to rise in the coming years (2).

In spite of the considerable public health significance of the disease, little is known about the etiology of NHL. The established risk factors for NHL are primary, acquired, or iatrogenic immunodeficiencies, but these conditions are extremely rare and have not increased in prevalence during the past decades (3). While the epidemic of acquired immunodeficiency syndrome has contributed to much of the recent increase in young people, it cannot explain the observed long-term increase in incidence among the elderly (4). Therefore, NHL differs from the two other cancers for which incidence rates are increasing rapidly, melanoma and lung cancer, in that the risk factors responsible for its increasing incidence are largely unknown.

Several recent epidemiologic studies have suggested that dietary factors influence NHL risk. For example, four studies have proposed an increased risk of NHL associated with

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milk intake (5–9), while others have not (10–12). An inverse association was observed for intakes of whole-grain foods (5, 8) and for higher intakes of vegetables (6, 8, 10, 13) and citrus fruits (6, 10). More recent studies have suggested that saturated fat (10, 12) and animal protein intakes (10) may be associated with the risk of NHL. An increased risk of NHL associated with high protein and fat intakes is biologically plausible because diets high in protein and fat may lead to altered immunocompetence, and immune system impairment is the only established risk factor for NHL (14). A reduced risk of NHL associated with vegetable and fruit intake is also biologically plausible because of the antioxidant properties of these foods or their ability to inhibit nitrosation reactions (14).

Although these earlier epidemiologic studies have provided new leads linking diet and nutrient intakes to the risk of NHL, few have systematically examined the relation. One study examined the associations by NHL subtype (6), despite the evidence indicating that NHL subtypes may be etiologically distinct. Considering the uncertainty regarding the role of diet and nutrients on the risk of NHL and the rapid increase in the disease, we conducted a population-based case-control study in Connecticut in 1995–2001 to evaluate the association of NHL with diet and nutrients, specifically animal proteins, fat, vegetables, and fruits.

MATERIALS AND METHODS

Study population

Cases were histologically confirmed, incident NHL patients (*International Classification of Diseases for Oncology* (15), M-9590–9595, 9670–9687, 9690–9698, 9700–9723) diagnosed in Connecticut between 1996 and 2000. Subjects were restricted to women who were aged 21–84 years at diagnosis, had no previous diagnosis of cancer except nonmelanoma skin cancer, and were alive at the time of interview. Cases were identified through the Yale Comprehensive Cancer Center's Rapid Case Ascertainment Shared Resource, which acts as an agent of the Connecticut Tumor Registry. The Connecticut Public Health Code requires reporting of cancers from licensed hospitals and clinical laboratories to the Connecticut Tumor Registry. Field staffs of Rapid Case Ascertainment are assigned geographically to survey all of the state's nonpediatric hospitals to identify newly diagnosed cases. Information on cases identified in the field is sent regularly to the Rapid Case Ascertainment data entry staff, where the case's demographic data are entered, verified, and screened against the Connecticut Tumor Registry database. The Connecticut Tumor Registry has reciprocal reporting agreements with cancer registries in all adjacent states (and Florida) to identify Connecticut residents with cancer diagnosed and/or treated in these states. A total of 832 incident NHL cases were identified during the study period, with 601 of them (72 percent) completing in-person interviews.

To provide accurate and consistent histologic classification of the cases, pathology slides (or tissue blocks) were obtained for all cases from the pathology departments in which each was diagnosed. The specimens were reviewed by two study pathologists (S. F. and G. T.) experienced in the diagnosis of lymphoma. The NHL cases were classified according to the Working Formulation by grade (low, intermediate, or high), histologic type (diffuse or follicular), and immunologic type (B cell or T cell).

Population-based controls with Connecticut addresses were recruited by using random digit dialing methods for those below age 65 years or Health Care Financing Administration files for those aged 65 years or older. The participation rate for controls identified via random digit dialing was 69 percent, and it was 47 percent for Health Care Financing Administration controls. Cases and controls were frequency matched by age in 5-year intervals by adjusting the number of controls randomly selected in each age stratum every few months.

Interviews

All procedures were performed in accordance with a protocol approved by the Human Investigations Committee at Yale University and the Connecticut Department of Public Health and by the National Cancer Institute Special Studies Institutional Review Board. After approval from the hospitals and from each subject's physician (for cases) was obtained, or following selection through random sampling (for controls), potential participants were approached by letter and then by telephone. Those who agreed were interviewed by trained study personnel at the subject's home or at another convenient location. A standardized, structured questionnaire elicited demographic information and other major known or suspected risk factors that might confound the association between dietary intakes and risk of NHL. A semiquantitative food frequency questionnaire developed by the Fred Hutchinson Cancer Research Center (Seattle, Washington) was completed by each subject, who was asked to characterize her usual diet in the year prior to being interviewed, with the understanding that this information is very highly correlated with diet in the more distant past (16). The food frequency questionnaire collects data on consumption frequency and portion size for approximately 120 foods and beverages and is updated periodically to reflect US food consumption patterns and major market changes. This questionnaire has been validated and was designed to optimize estimation of fat intake (17). After completion, the food frequency questionnaire was sent to the Fred Hutchinson Cancer Research Center for analysis. Average daily nutrient intakes were calculated by using the University of Minnesota Nutrition Coding Center Nutrient Data System database.

Data analysis

Unconditional logistic regression was used to estimate the association between the risk of NHL and intakes of macro- and micronutrients and various food items. For each macro- or micronutrient index, quartiles of consumption were produced by dividing the frequency distribution of the control group at the 25th, 50th, and 75th percentiles. The statistical model used to assess the effect of calorie-providing nutrient intakes was suggested by Willett and Stampfer (18). In this model, calculated macronutrient

TABLE 1. Selected baseline characteristics of NHL* cases and controls, Connecticut, 1995–2001

Characteristic	Cases		Controls	
	No.	%	No.	%
Age (years)				
<50	119	19.8	155	21.6
50–70	277	46.1	317	44.2
>70	205	34.1	245	34.2
Race				
White	571	95.0	667	93.0
Black	18	3.0	25	3.5
Other	12	2.0	25	3.5
Family history of NHL in first-degree relatives				
No	592	98.5	713	99.4
Yes	9	1.5	4	0.6
Tobacco smoking				
Never	270	44.9	323	45.0
Ever	331	55.1	394	55.0
Alcohol drinking				
Never	228	37.9	231	32.2
Ever	371	61.8	484	67.5
Unknown	2	0.3	2	0.3
Educational level				
High school or less	261	43.4	265	37.0
Some college or higher	340	56.6	452	63.0

* NHL, non-Hodgkin's lymphoma.

intakes were adjusted by taking the residual from a linear, least-squares regression model in which total energy intake was the dependent variable and the macronutrient was the independent variable. The analysis of micronutrient and food item intakes was adjusted for total energy intake as a categorical variable (<1,269, 1,269–1,595, 1,596–1,947, >1,947 kcal). Adjustment by total energy intake as a continuous variable in the model produced similar results.

The following confounding variables were also included in the final model: age (in years as a continuous variable), body mass index (weight (kg)/height $(m)^2$: <22, 22–24.5, 24.6–28, >28), and family history of NHL in first-degree relatives. Adjustments of other variables (such as race (White, Black, other), level of education (high school or less, some college or higher), tobacco smoking (ever/never), alcohol consumption (ever/never)) did not result in material changes for the observed associations and thus were not included in the final model. Odds ratios and 95 percent confidence intervals were calculated by using SAS statistical software (19).

RESULTS

Table 1 presents selected characteristics of the cases and controls. Cases and controls were similar in age at diagnosis because of frequency matching. However, more cases than controls reported a family history of NHL. Controls, on the other hand, had a slightly higher level of education and alcohol intake. The distribution of other factors (such as race and tobacco smoking) was similar between the cases and the controls.

Table 2 describes the association between risk of NHL and macronutrient intakes by type of NHL. Daily consumption of protein was associated with an increased risk of NHL. However, the increased risk associated with protein intake appeared to be associated mainly with animal sources, not with vegetable protein consumption. Total daily fat intake was also associated with an increased risk of NHL. This increase in risk came mainly from saturated fat. Polyunsaturated fat was actually associated with a 40 percent reduced risk. The results by NHL subtype (table 3) show that the increased risk associated with animal protein intake was seen for both diffuse and follicular lymphoma, B-cell, and intermediate/high-grade NHL. Saturated fat was associated with a significantly increased risk of diffuse lymphoma, B-cell lymphoma, and intermediate/high-grade lymphoma. Total daily carbohydrate intake was also associated with significantly increased risks of diffuse and intermediate/high-grade NHL at the higher intake levels.

As shown in table 4, total vitamin A, β-carotene, α-carotene, and vitamin C intakes did not show an association with NHL risk, whereas retinol showed a 40 percent increased risk at the highest intake level (odds ratio (OR) = 1.4, 95 percent confidence interval (CI): 1.0, 2.1). A significantly reduced risk of NHL was observed for dietary fiber intakes at the highest intake level (OR = 0.6, 95 percent CI: 0.4, 0.8). Both water-soluble dietary fiber and water-insoluble dietary fiber showed a similar reduced risk. Consumption of vitamin E, vitamin D, iron, and other trace metals was not found to be associated with the risk of NHL in this study (data not shown). The results by NHL subtype (table 5) showed that retinol intake at the highest quartile was associated with a significantly increased risk for intermediate/high-grade NHL (OR = 1.8, 95 percent CI: 1.1, 3.0). On the other hand, α-carotene showed a significantly reduced risk at the highest intake level for diffuse lymphoma (OR = 0.6, 95 percent CI: 0.4, 0.9). Dietary fiber intake at the highest intake level was associated with significantly reduced risks of diffuse, B-cell, and intermediate/high-grade NHL, and both water-soluble and insoluble dietary fiber showed similar risk patterns by NHL subtype.

In this study, dietary intakes of vegetables as a group or carotene-rich vegetables specifically (including carrots, squash, and yams) were not associated with a risk of NHL (data not shown). However, a higher intake of cruciferous vegetables (including broccoli, cabbage, cauliflower, and brussels sprouts) was associated with a significantly reduced risk (OR = 0.7, 95 percent CI: 0.5, 0.9) for women whose consumption frequency was greater than or equal to twice per week compared with those whose frequency of consumption was less than twice per month. Intake of dairy products (including milk, ice cream, milkshakes, creamed soups, butter, cheeses, yogurt, and margarine), on the other hand, was associated with a significantly increased risk of NHL (OR = 1.8, 95 percent CI: 1.2, 2.8) for women whose

TABLE 2. Risk of NHL* associated with macronutrients for Connecticut women, 1995–2001

Macronutrient	Cases (no.)	Controls (no.)	OR*,†	95% CI*	*p* for trend
Total protein (g)					
<46	122	173	1.0		
46–57	142	183	1.1	0.8, 1.5	
58–72	159	177	1.2	0.9, 1.7	
>72	171	177	1.4	1.0, 1.9	0.26
Animal protein (g)‡					
<31	124	183	1.0		
31–39	142	179	1.2	0.8, 1.6	
40–52	157	171	1.5	1.1, 2.1	
>52	171	177	1.7	1.2, 2.4	0.05
Vegetable protein (g)§					
<14	154	194	1.0		
14–17	146	168	1.0	0.8, 1.4	
18–21	145	176	0.9	0.7, 1.3	
>21	149	172	1.0	0.7, 1.4	0.96
Total fat (g)					
<50	129	178	1.0		
50–66	125	180	1.0	0.7, 1.3	
67–85	154	175	1.2	0.9, 1.6	
>85	186	177	1.4	1.0, 1.9	0.04
Saturated fat (g)¶					
<17	113	169	1.0		
17–23	148	187	1.3	0.9, 1.9	
24–30	128	179	1.1	0.7, 1.8	
>30	205	175	1.9	1.1, 2.3	0.03
Monounsaturated fat (g)#					
<18	141	191	1.0		
18–23	124	172	1.0	0.7, 1.4	
24–30	164	180	1.2	0.8, 1.7	
>30	165	167	1.2	0.7, 2.0	0.89
Polyunsaturated fat (g)**					
<12	172	198	1.0		
12–15	139	186	0.7	0.5, 1.0	
16–20	144	159	0.8	0.5, 1.1	
>20	139	167	0.6	0.4, 0.9	0.06
Total carbohydrate (g)					
<140	118	177	1.0		
140–178	138	176	1.2	0.8, 1.6	
179–227	165	180	1.4	1.0, 1.9	
>227	173	177	1.4	1.0, 2.0	0.01

* NHL, non-Hodgkin's lymphoma; OR, odds ratio; CI, confidence interval.

† Adjusted for age (as a continuous variable), body mass index (weight (kg)/height $(m)^2$: <22, 22–24.5, 24.6–28, >28), and family history of NHL in first-degree relatives.

‡ Additional adjustment for vegetable protein intake.

§ Additional adjustment for animal protein intake.

¶ Additional adjustment for monounsaturated fat and polyunsaturated fat intake.

Additional adjustment for saturated fat and polyunsaturated fat intake.

** Additional adjustment for saturated fat and monounsaturated fat intake.

TABLE 3. Risk of NHL* associated with macronutrients, by NHL subtypes, for Connecticut women, 1995–2001

Macronutrient	Histology						Immunologic cell type						Grade					
	Follicular			Diffuse			B cell			T cell			Low			Intermediate/high		
	Cases (no.)	OR*,†	95% CI*	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI
Total protein (g)																		
<46	26	1.0		63	1.0		89	1.0		14	1.0		42	1.0		47	1.0	
46–57	32	1.2	0.7, 2.0	86	1.3	0.9, 1.9	118	1.2	0.9, 1.8	8	0.6	0.2, 1.4	38	0.9	0.5, 1.4	80	1.6	1.1, 2.5
58–72	36	1.2	0.7, 2.1	98	1.5	1.0, 2.3	131	1.4	1.0, 2.0	11	0.7	0.3, 1.6	48	1.1	0.7, 1.7	86	1.8	1.2, 2.7
>72	38	1.3	0.8, 2.3	97	1.5	1.0, 2.2	131	1.4	1.0, 2.0	11	0.7	0.3, 1.5	48	1.1	0.7, 1.8	88	1.8	1.2, 2.7
p for trend			0.61			0.26			0.31			0.36			0.95			0.11
Animal protein (g)‡																		
<31	24	1.0		66	1.0		86	1.0		14	1.0		41	1.0		49	1.0	
31–39	34	1.5	0.9, 2.7	83	1.3	0.9, 2.0	116	1.4	1.0, 2.1	10	0.7	0.3, 1.7	40	1.0	0.6, 1.7	77	1.7	1.1, 2.6
40–52	36	1.8	1.0, 3.3	97	1.8	1.2, 2.7	135	1.9	1.3, 2.8	9	0.7	0.3, 1.7	47	1.3	0.8, 2.2	86	2.3	1.5, 3.5
>52	38	2.1	1.1, 3.9	98	1.9	1.2, 2.9	132	2.0	1.4, 3.1	11	0.7	0.2, 1.8	48	1.3	0.8, 2.3	89	2.5	1.5, 4.0
p for trend			0.14			0.06			0.02			0.26			0.77			0.01
Vegetable protein (g)§																		
<14	36	1.0		82	1.0		122	1.0		12	1.0		45	1.0		73	1.0	
14–17	31	0.9	0.5, 1.6	95	1.2	0.8, 1.8	121	1.0	0.7, 1.5	9	1.0	0.4, 2.5	45	1.1	0.7, 1.8	81	1.1	0.8, 1.7
18–21	37	1.0	0.6, 1.8	82	1.0	0.6, 1.4	114	0.9	0.6, 1.2	12	1.4	0.6, 3.6	42	1.0	0.6, 1.6	77	1.0	0.6, 1.5
>21	28	0.8	0.4, 1.5	85	1.0	0.7, 1.6	112	0.9	0.6, 1.3	11	1.2	0.4, 3.2	44	1.1	0.6, 1.9	70	0.9	0.6, 1.4
p for trend			0.83			0.78			0.49			0.43			0.75			0.87
Total fat (g)																		
<51	29	1.0		68	1.0		100	1.0		9	1.0		45	1.0		52	1.0	
51–68	26	0.9	0.5, 1.6	73	1.1	0.7, 1.6	99	1.0	0.7, 1.4	13	1.2	0.5, 2.9	36	0.8	0.5, 1.3	63	1.2	0.8, 1.8
69–87	34	1.1	0.7, 2.0	94	1.4	0.9, 2.0	123	1.2	0.9, 1.7	13	1.2	0.5, 3.0	39	0.9	0.5, 1.4	89	1.7	1.1, 2.5
>87	43	1.4	0.8, 2.3	109	1.6	1.1, 2.3	147	1.4	1.0, 2.0	9	0.8	0.3, 2.2	56	1.2	0.8, 1.9	97	1.8	1.2, 2.7
p for trend			0.11			0.06			0.03			0.37			0.28			0.02

Table continues

consumption frequency was greater than or equal to twice per day compared with those whose frequency of consumption was less than three times per week. No other food groups (such as all fruits, meats, red meat, all fish) were significantly associated with NHL risk at the highest intake levels.

Table 6 presents information on specific food items associated with a significant or borderline significantly (upper 95 percent CI: ≤1.0) reduced risk of NHL. Among fruits, only citrus (oranges, grapefruit, or tangerines), apples, and pears were associated with a reduced risk of NHL. On the other hand, several vegetables were associated with a significantly reduced risk of NHL, particularly tomatoes, broccoli, squash, cabbage, brussels sprouts, cauliflower, onions, leeks, and mixed lettuce salad with vegetables. Higher intakes of tuna, dark breads, tortillas, popcorn, and mayonnaise were also associated with a significantly reduced risk of NHL.

Table 7 presents data on specific food items associated with a significantly or borderline significantly (lower 95 percent CI: ≥1.0) increased risk of NHL. Egg intake at the highest intake level was associated with an increased risk of NHL (OR = 1.4, 95 percent CI: 1.0, 2.0). Intakes of several dairy products were associated with an increased risk at the highest intake level: milk (OR = 1.6, 95 percent CI: 1.0, 2.3), butter or margarine on bread (OR = 1.6, 95 percent CI: 1.1, 2.3), cream soups (OR = 1.6, 95 percent CI: 1.0, 2.5), and ice cream or milkshakes (OR = 1.5, 95 percent CI: 1.1, 2.1). Greater consumption of cheese, yogurt, and mayonnaise was not found to be associated with an increased risk (data not shown). An increased risk was also observed for intakes of sweet potatoes at the third quartile (OR = 1.6, 95 percent CI: 1.2, 2.2) and white bread at the highest intake level (OR = 1.5, 95 percent CI: 1.0, 2.0).

DISCUSSION

In this population-based case-control study, we found an increased risk of NHL associated with higher consumption of animal protein, saturated fat, and carbohydrates. An increased risk was also observed for higher consumption of eggs and dairy products (including milk and butter products) and white bread. On the other hand, a significantly reduced

TABLE 3. Continued

Macronutrient	Histology						Immunologic cell type						Grade					
	Follicular			Diffuse			B cell			T cell			Low			Intermediate/high		
	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI
Saturated fat (g)¶																		
<17	27	1.0		56	1.0		86	1.0		10	1.0		41	1.0		42	1.0	
17–23	32	1.0	0.5, 1.9	88	1.7	1.1, 2.7	114	1.4	0.9, 2.1	15	1.2	0.4, 3.3	43	1.1	0.6, 2.0	77	1.7	1.1, 2.9
24–31	30	0.8	0.4, 1.6	80	1.5	0.9, 2.5	109	1.3	0.8, 2.1	9	0.7	0.2, 2.3	38	0.8	0.4, 1.6	72	1.7	1.0, 2.9
>31	43	1.1	0.4, 2.6	120	2.3	1.2, 4.3	160	2.0	1.2, 3.6	10	0.9	0.2, 4.3	54	1.0	0.4, 2.2	110	2.8	1.5, 5.5
p for trend			0.70			0.04			0.03			0.98			0.65			0.02
Monounsaturated fat (g)#																		
<17	32	1.0		74	1.0		108	1.0		12	1.0		50	1.0		56	1.0	
17–22	23	0.9	0.5, 1.6	74	1.0	0.7, 1.6	98	1.0	0.6, 1.4	12	1.1	0.4, 2.7	31	0.9	0.5, 1.5	66	1.0	0.7, 1.6
23–29	40	1.4	0.8, 2.5	100	1.2	0.8, 1.8	131	1.1	0.8, 1.6	12	1.2	0.5, 3.1	47	1.3	0.8, 2.2	93	1.2	0.8, 1.9
>29	37	1.3	0.5, 3.2	96	1.3	0.7, 2.5	132	1.1	0.6, 2.0	8	1.1	0.2, 5.2	48	1.6	0.7, 3.7	86	1.2	0.6, 2.2
p for trend			0.90			0.99			0.89			0.94			0.89			0.82
Polyunsaturated fat (g)**																		
<11	31	1.0		102	1.0		135	1.0		12	1.0		55	1.0		78	1.0	
11–14	33	1.1	0.6, 1.9	74	0.6	0.4, 0.8	107	0.7	0.5, 1.0	14	1.2	0.5, 2.9	34	0.8	0.6, >19	73	0.7	0.5, 1.1
15–19	30	1.0	0.5, 2.0	92	0.8	0.5, 1.2	114	0.8	0.5, 1.2	11	1.2	0.4, 3.4	38	0.7	0.4, 1.3	84	0.9	0.5, 1.4
>19	38	1.1	0.5, 2.3	76	0.5	0.3, 0.8	113	0.6	0.4, 1.0	7	0.7	0.2, 2.7	49	1.0	0.4, 1.5	66	0.5	0.3, 0.9
p for trend			0.57			0.02			0.11			0.66			0.64			0.06
Total carbohydrate (g)																		
<140	28	1.0		59	1.0		90	1.0		8			39	1.0		48	1.0	
140–178	26	0.9	0.5, 1.7	90	1.5	1.0, 2.2	112	1.2	0.9, 1.8	9	1.0	0.4, 2.7	39	1.0	0.6, 1.6	77	1.6	1.0, 2.4
179–227	41	1.4	0.9, 2.5	99	1.6	1.1, 2.4	133	1.3	1.0, 2.1	14	1.6	0.7, 4.1	51	1.3	0.8, 2.1	89	1.8	1.2, 2.8
>227	37	1.3	0.8, 2.2	96	1.6	1.1, 2.3	134	1.4	1.0, 2.0	13	1.5	0.6, 3.8	47	1.2	0.7, 1.9	87	1.7	1.2, 2.6
p for trend			0.04			0.02			0.01			0.37			0.12			0.01

* NHL, non-Hodgkin's lymphoma; OR, odds ratio; CI, confidence interval.

† Adjusted for age (as a continuous variable), body mass index (weight (kg)/height (m)^2: <22, 22–24.5, 24.6–28, >28), and family history of NHL in first-degree relatives.

‡ Additional adjustment for vegetable protein intake.

§ Additional adjustment for animal protein intake.

¶ Additional adjustment for monounsaturated fat and polyunsaturated fat intake.

Additional adjustment for saturated fat and polyunsaturated fat intake.

** Additional adjustment for saturated fat and monounsaturated fat intake.

risk was observed for a greater intake of dietary fiber, tomatoes, broccoli, squash, cabbage, cauliflower, onions, leeks, mixed lettuce salad with vegetables (such as carrots, tomatoes), dark bread, tortillas, popcorn, citrus fruits, apples, and pears.

It has been suggested that higher intakes of protein may increase the risk of NHL through effects on the immune system, as reviewed by Chiu et al. (10). Excessive absorption of animal protein could lead to chronic hyperstimulation of the immune system (9) and increased immune unresponsiveness (20, 21). An international correlation study by Cunningham (9) reported a strong positive correlation between per capita animal protein consumption and lymphoma mortality rates ($r = 0.70$, $p < 0.01$). Three epidemiologic studies reported a significantly increased risk of NHL associated with milk intake (5, 7, 8). Among the three analytical epidemiologic studies that directly investigated dietary protein intake and risk of NHL, Chiu et al. reported a nonsignificantly increased risk of NHL associated with animal protein intake (OR = 1.5, 95 percent CI: 0.9, 2.4), with no association for vegetable protein intake (OR = 1.0, 95 percent CI: 0.6, 1.5). Two other studies, however, found no association between NHL risk and animal or vegetable protein intake (6, 12).

As recently reviewed by others (10, 14), fat in the diet may also influence immune function either by actions on the cyclooxygenase, lipoxygenase, or cytochrome P-450 pathways or directly on cell function through its effects on cell membrane structure and function. Alteration in dietary fat concentration or level of saturation was found to alter

TABLE 4. Risk of NHL* associated with micronutrients for Connecticut women, 1995–2001

Micronutrient	Cases (no.)	Controls (no.)	OR*,†	95% CI*	*p* for trend
Total vitamin A (IU)					
<5,423	135	178	1.0		
5,423–7,444	129	177	0.9	0.6, 1.2	
7,445–10,618	159	178	1.0	0.7, 1.4	
>10,618	147	177	0.9	0.6, 1.3	0.96
Retinol (μg)					
<302	116	177	1.0		
302–450	143	179	1.2	0.9, 1.7	
451–640	142	177	1.1	0.7, 1.6	
>640	193	177	1.4	1.0, 2.1	0.49
Beta-carotene (μg)					
<2,049	142	177	1.0		
2,049–2,994	143	178	0.9	0.7, 1.3	
2,995–4,471	156	178	1.0	0.7, 1.3	
>4,471	153	177	1.0	0.7, 1.4	0.80
Alpha-carotene (μg)					
<473	161	177	1.0		
473–731	139	179	0.8	0.6, 1.1	
732–1,082	151	176	0.9	0.6, 1.2	
>1,082	143	178	0.8	0.6, 1.1	0.13
Vitamin C (mg)					
<67	143	177	1.0		
67–103	133	177	0.9	0.6, 1.2	
104–139	154	177	1.0	0.7, 1.4	
>139	164	179	1.0	0.7, 1.4	0.46
Dietary fiber (g)					
<10.8	150	181	1.0		
10.8–14.3	173	179	1.0	0.7, 1.3	
14.4–18.3	145	175	0.7	0.5, 1.1	
>18.3	126	176	0.6	0.4, 0.8	0.02
Water-soluble dietary fiber (g)					
<3.9	140	175	1.0		
3.9–5.1	188	190	1.1	0.8, 1.5	
5.2–6.4	129	169	0.7	0.5, 1.0	
>6.4	137	176	0.6	0.4, 1.0	0.10
Water-insoluble dietary fiber (g)					
<6.8	151	177	1.0		
6.8–9.1	163	177	0.9	0.7, 1.3	
9.2–11.9	154	182	0.8	0.5, 1.1	
>11.9	126	174	0.6	0.4, 0.9	0.01

* NHL, non-Hodgkin's lymphoma; OR, odds ratio; CI, confidence interval.

† Adjusted for age, body mass index (weight (kg)/height $(m)^2$: <22, 22–24.5, 24.6–28, >28), family history of NHL in first-degree relatives, total energy intake (<1,269, 1,269–1,595, 1,596–1,947, >1,947 kcal), animal protein intake (quartile), saturated fat intake (quartile), and polyunsaturated fat intake (quartile).

membrane phospholipid fatty acid composition in a variety of cellular and subcellular membranes; such alterations, if in lymphocytes, could lead to impaired immune function (10). Two previous studies examined dietary intakes of specific types of fats and risk of NHL. Similar to our study, one by Chiu et al. (10) reported a significantly increased risk of NHL associated with animal fat intake (relative risk (RR) = 2.0, 95 percent CI: 1.2, 3.3) and saturated fat intake (RR = 1.7, 95 percent CI: 1.1, 2.7) but not polyunsaturated fat intake (RR = 1.1, 95 percent CI: 0.7, 1.8) when the highest tertile of intake was compared with the lowest (no actual intake level was reported). Zhang et al. (12) reported an increased risk of NHL associated with higher intakes of transunsaturated fat (RR = 2.4, 95 percent CI: 1.3, 4.6) and, perhaps, saturated fat (RR = 1.4, 95 percent CI: 0.7, 3.0) when the highest quintile of intake was compared with the lowest (no actual intake level was reported). It is interesting to note that white bread, one of the major sources of transunsaturated fat intake, was associated with an increased risk of NHL in our study. Ward et al. (6) also found that bread and cereal consumption was associated positively with NHL risk. However, the study did not distinguish between types of breads and cereals.

Chiu et al. (10) reported a significant trend for NHL risk and red meat consumption (RR = 1.7, $p_{trend} = 0.04$). In that study, analysis of consumption of specific items in the red meat group showed that hamburger was the only food item associated with increased NHL risk. Our study did not show an increased risk of NHL associated with red meat intake, however. An odds ratio of 0.8 (95 percent CI: 0.5, 1.1) was observed for consumption of hamburger when the highest level of intake was compared with the lowest. However, as reviewed by Chiu et al., carcinogens and mutagens such as heterocyclic amines can be generated during the cooking of red meat, and feeding experiments have shown that these compounds can induce immunotoxicity and lymphomas. Further investigation of the relation between red meat intake and risk of NHL is warranted

One of the major findings from our study was an increased risk of NHL associated with higher consumption of eggs and dairy products. Of seven previous analytical epidemiologic studies that investigated the association between dietary intakes and NHL risk, three found a significantly increased risk of NHL associated with milk intake (5, 7, 8) while the remaining four found no significant association (6, 10–12). Ross and Bras (22) have reported an increased risk of lymphomas in experimental rats after augmentation of the diet with casein, the major protein found in milk. Milk and other dairy products are important sources of fat and vitamin A. Similar to our study, one by Tavani et al. (5) also reported a statistically significantly increased risk of NHL associated with retinol intake, with an odds ratio of 2.4 ($p < 0.05$) for the highest tertile of intake compared with the lowest. Middleton et al. (23) also reported an increased risk of Hodgkin's disease associated with vitamin A intake, calculated largely on the basis of milk and vegetable consumption. It has been suggested that a bovine leukemia virus, which can cause lymphosarcomas in cattle, can be transmitted through milk to humans (24). However, no study has demonstrated that the virus can actually infect humans (25). The data from three large cohort studies in the United States (the Nurses' Health Study, the Health Professionals Follow-up Study, and the Cancer Prevention Study II) do not support a relation between dietary intake of vitamins A (including carotenoids), C, or E (13) or use of individual supplements of vitamins A, C, and E or multivitamins and the risk of NHL (26, 27).

In our study, a higher dietary fiber intake was associated with a significantly reduced risk of NHL. Few previous studies have investigated specific fiber intakes and NHL risk. Chiu et al. (10) reported a nonsignificantly reduced risk of NHL associated with dietary fiber intake for moderate intake levels (OR = 0.77, 95 percent CI: 0.48, 1.25) and for high intake (OR = 0.86, 95 percent CI: 0.54, 1.36) when compared with low intake. A recent report of the Nurses' Health Study found that intake of dietary fiber from vegetable sources was related to a significantly reduced risk (OR = 0.5, 95 percent CI: 0.3, 0.9) for women in the highest quintile compared with those in the lowest (13). Tavani et al. (5) reported a significantly reduced risk of NHL associated with higher consumption of whole-grain foods (OR = 0.4, $p < 0.05$), an important source of fiber. An earlier case-control study by Franceschi et al. (8) also reported a reduced risk of NHL associated with whole-grain bread or pasta intake. An odds ratio of 0.53 was reported when the highest intake was compared with the lowest ($p_{trend} < 0.05$). To explain the observed inverse association between fiber intakes and NHL risk, Franceschi et al. (8) hypothesized that alimentary fibers may affect the dilution, absorption, and/or breakdown of fat and animal protein in the gut, either directly or indirectly by modifying the gut microflora composition.

Another major finding of our study was that higher intakes of tomatoes, broccoli, squash, cauliflower, onions, and mixed lettuce salad were associated with a significantly reduced risk of NHL. The Nurses' Health Study (13) also reported that higher intake of cruciferous vegetables was associated with a decreased risk of NHL ($p_{trend} = 0.02$). In that study, a relative risk of 0.6 (95 percent CI: 0.4, 0.9) was observed for a combination intake of cabbage, cauliflower, and brussels sprouts for consumption frequencies greater than or equal to two servings per week compared with less than one serving per week. Ward et al. (6) reported that of various dark green vegetables (including broccoli, green beans, kale/collard and turnip greens), broccoli intake was associated with a decreased risk of NHL.

It is hypothesized that the antioxidant properties of vegetables and fruits or their ability to inhibit nitrosation reactions may protect against NHL. We found a reduced risk of NHL associated with intake of citrus fruit (in the middle categories), apples, and pears in this study. The study by Ward et al. (6) also reported a significantly decreased risk of NHL for men associated with high levels of consumption of citrus fruits, including oranges/grapefruits and orange/grapefruit juices, and the risks decreased with increasing intake (p for trend = 0.003). However, no significant association was found for women in Ward's study. A significantly reduced risk of NHL for higher intake of all fruits was reported by Chiu et al. (10). A nonsignificantly reduced risk of NHL for the higher intakes of all fruits was reported by De Stefani et

TABLE 5. Risk of NHL* associated with micronutrients, by NHL subtypes, for Connecticut women, 1995–2001

Micronutrient	Histology						Immunologic cell type						Grade					
	Follicular			Diffuse			B cell			T cell			Low			Intermediate/high		
	Cases (no.)	OR*,†	95% CI*	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI
Total vitamin A (IU)																		
<5,423	23	1.0		88	1.0		113	1.0		9	1.0		36	1.0		75	1.0	
5,423–7,444	30	1.3	0.7, 2.3	74	0.7	0.5, 1.1	102	0.8	0.6, 1.1	13	1.6	0.6, 4.0	41	1.1	0.6, 1.8	63	0.7	0.5, 1.1
7,445–10,618	44	1.8	1.0, 3.3	87	0.8	0.5, 1.1	126	0.9	0.6, 1.3	10	1.0	0.3, 2.7	47	1.2	0.7, 2.1	84	0.8	0.5, 1.2
>10,618	32	1.3	0.7, 2.6	78	0.7	0.4, 1.0	114	0.8	0.6, 1.2	7	0.7	0.2, 2.2	47	1.2	0.7, 2.2	64	0.6	0.4, 1.0
p for trend			0.47			0.12			0.54			0.45			0.47			0.11
Retinol (μg)																		
<302	24	1.0		62	1.0		83	1.0		11	1.0		36	1.0		50	1.0	
302–450	31	1.3	0.7, 2.4	82	1.3	0.8, 1.9	117	1.4	0.9, 2.0	11	1.3	0.5, 3.4	43	1.2	0.7, 2.1	70	1.3	0.8, 2.1
451–640	33	1.3	0.7, 2.6	83	1.1	0.7, 1.8	116	1.2	0.8, 1.8	7	0.9	0.3, 3.0	44	1.2	0.7, 2.1	72	1.2	0.7, 1.9
>640	44	1.7	0.8, 3.4	117	1.6	1.0, 2.6	153	1.6	1.0, 2.4	15	2.2	0.8, 6.7	53	1.3	0.7, 2.4	109	1.8	1.1, 3.0
p for trend			0.08			0.97			0.45			0.64			0.27			0.70
Beta-carotene (μg)																		
<2,049	26	1.0		90	1.0		117	1.0		11	1.0		35	1.0		81	1.0	
2,049–2,994	26	0.9	0.5, 1.7	93	0.9	0.6, 1.3	116	0.9	0.6, 1.3	11	1.0	0.4, 2.4	46	1.2	0.8, 2.1	73	0.8	0.5, 1.2
2,995–4,471	46	1.6	0.9, 2.9	82	0.7	0.5, 1.1	122	0.9	0.6, 1.3	14	1.2	0.5, 3.0	44	1.2	0.7, 2.0	84	0.8	0.6, 1.2
>4,471	34	1.3	0.7, 2.3	79	0.7	0.5, 1.1	114	0.9	0.6, 1.3	8	0.6	0.2, 1.8	51	1.4	0.8, 2.4	63	0.6	0.4, 1.0
p for trend			0.64			0.28			0.67			0.48			0.28			0.12
Alpha-carotene (μg)																		
<473	30	1.0		99	1.0		129	1.0		16	1.0		41	1.0		88	1.0	
473–731	31	0.9	0.5, 1.6	84	0.7	0.5, 1.1	110	0.8	0.5, 1.1	12	0.8	0.3, 1.8	46	1.0	0.6, 1.7	69	0.7	0.5, 1.0
732–1,082	34	1.1	0.6, 1.9	87	0.8	0.5, 1.1	120	0.9	0.6, 1.2	6	0.4	0.1, 1.0	44	1.0	0.6, 1.7	77	0.8	0.5, 1.2
>1,082	37	1.1	0.6, 2.0	74	0.6	0.4, 0.9	110	0.8	0.5, 1.1	10	0.6	0.2, 1.5	45	1.0	0.6, 1.7	67	0.6	0.4, 1.0
p for trend			0.59			0.03			0.09			0.40			0.98			0.01

Table continues

al. (11) (OR = 0.78, 95 percent CI: 0.33, 1.83) and by Tavani et al. (5) (OR = 0.9, $p > 0.05$). The Nurses' Health Study also reported a nonsignificantly reduced risk of NHL associated with fruit intake. In that study, citrus fruit intake was not associated with NHL risk (13).

In his review of nutritional factors and the risk of NHL for a 1992 meeting sponsored by the National Cancer Institute ("The Emerging Epidemic of NHL"), Davis pointed out that "future studies must be designed to investigate specific histologic subtypes of lymphoma or groupings of related types, for it may be that dietary influences are somewhat specific in their action" (28, p. 5494s). Our study results indicate that the risk of NHL associated with various dietary intakes may vary by NHL subtype. However, few other earlier studies have evaluated the association by NHL subtype because of various reasons, such as relatively small sample sizes. NHL represents a heterogenous group of lymphoid malignancies ranging in aggressiveness from very indolent cellular proliferation to highly aggressive and rapidly proliferative processes. It is possible that specific subgroups of the disease may have different etiologic profiles. Epidemiologic studies of other exposures, such as hair dye products, occupational exposures, and viruses, have shown that the risk of NHL associated with these exposures may vary by NHL subtype (29–33). Further investigation of the relation between dietary intake and NHL risk by NHL subtype is warranted.

A major advantage of our study is that the food frequency questionnaire we used was specifically developed by the Fred Hutchinson Cancer Research Center to evaluate dietary intakes and women's health. The questionnaire has been validated and was designed to optimize estimation of fat intake, one of the major hypotheses of the study. However, unlike prospective follow-up studies, for which data on dietary intakes are collected long before disease diagnosis, case-control studies rely on retrospective recall by study subjects through a food frequency questionnaire to estimate dietary intakes, which would undoubtedly introduce

TABLE 5. Continued

Micronutrient	Histology						Immunologic cell type						Grade					
	Follicular			Diffuse			B cell			T cell			Low			Intermediate/high		
	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI	Cases (no.)	OR†	95% CI
Vitamin C (mg)																		
<67	32	1.0		79	1.0		116	1.0		9	1.0		51	1.0		63	1.0	
67–103	33	0.5	0.3, 1.0	89	1.0	0.7, 1.5	103	0.8	0.6, 1.2	14	1.6	0.6, 3.9	30	0.5	0.3, 0.9	80	1.1	0.8, 1.7
104–139	37	0.9	0.5, 1.6	92	1.0	0.7, 1.5	125	1.0	0.7, 1.4	9	1.0	0.4, 2.8	51	0.9	0.5, 1.4	78	1.1	0.7, 1.6
>139	30	0.9	0.5, 1.6	84	0.8	0.6, 1.3	125	0.9	0.6, 1.3	12	1.1	0.4, 2.9	44	0.7	0.4, 1.2	80	1.0	0.6, 1.6
p for trend			0.61			0.62			0.82			0.89			0.49			0.67
Dietary fiber (g)																		
<10.8	29	1.0		90	1.0		121	1.0		12	1.0		42	1.0		77	1.0	
10.8–14.3	37	0.9	0.6, 1.9	106	0.9	0.6, 1.3	139	0.9	0.7, 1.3	11	0.9	0.3, 2.2	51	1.1	0.6, 1.8	92	0.9	0.6, 1.3
14.4–18.3	34	0.9	0.5, 1.7	85	0.6	0.4, 1.0	116	0.7	0.5, 1.0	10	0.7	0.3, 2.0	42	0.9	0.5, 1.5	77	0.7	0.4, 1.0
>18.3	32	0.7	0.4, 1.5	63	0.4	0.2, 0.7	93	0.5	0.3, 0.7	11	0.7	0.2, 1.9	41	0.7	0.4, 1.4	55	0.4	0.2, 0.6
p for trend			0.10			0.004			0.002			0.85			0.18			0.003
Water-soluble dietary fiber (g)																		
<3.9	32	1.0		78	1.0		112	1.0		13	1.0		44	1.0		66	1.0	
3.9–5.1	33	0.8	0.4, 1.3	122	1.2	0.8, 1.7	153	1.0	0.7, 1.5	13	0.8	0.3, 2.0	48	0.9	0.5, 1.4	107	1.2	0.8, 1.8
5.2–6.4	37	0.8	0.4, 1.5	73	0.6	0.4, 1.0	104	0.7	0.5, 1.0	5	0.3	0.1, 1.0	44	0.8	0.5, 1.4	66	0.7	0.4, 1.0
>6.4	30	0.5	0.3, 1.1	71	0.5	0.3, 0.9	100	0.5	0.3, 0.8	13	0.6	0.2, 1.7	40	0.7	0.4, 1.2	62	0.5	0.3, 0.8
p for trend			0.37			0.01			0.01			0.84			0.30			0.01
Water-insoluble dietary fiber (g)																		
<6.8	31	1.0		89	1.0		121	1.0		12	1.0		43	1.0		77	1.0	
6.8–9.1	31	0.8	0.5, 1.5	102	0.9	0.6, 1.3	130	0.9	0.6, 1.3	10	0.8	0.3, 2.0	44	0.9	0.5, 1.5	89	0.9	0.6, 1.3
9.2–11.9	40	1.0	0.5, 1.8	86	0.7	0.4, 1.0	123	0.8	0.5, 1.1	10	0.7	0.3, 2.0	48	1.0	0.5, 1.6	78	0.7	0.4, 1.0
>11.9	30	0.6	0.3, 1.3	67	0.5	0.3, 0.7	95	0.5	0.3, 0.8	12	0.8	0.3, 2.2	41	0.8	0.4, 1.4	57	0.4	0.3, 0.7
p for trend			0.05			0.003			0.001			0.85			0.14			0.002

* NHL, non-Hodgkin's lymphoma; OR, odds ratio; CI, confidence interval.

† Adjusted for age, body mass index (weight (kg)/height $(m)^2$: <22, 22–24.5, 24.6–28, >28), family history of NHL in first-degree relatives, total energy intake (<1,269, 1,269–1,595, 1,596–1,947, >1,947 kcal), animal protein intake (quartile), saturated fat intake (quartile), and polyunsaturated fat intake (quartile).

misclassification of exposure. It is suggested that usual diet in the year prior to being interviewed is highly correlated with diet in the more distant past (16), and, since so little is known about the etiology of NHL, particularly the etiologic role of diet and nutrients in the risk of NHL, the misclassification should be nondifferential, and nondifferential misclassification of exposure would lead to underestimation of the observed association.

Another concern for population-based epidemiologic studies is the relatively low rate of participation by the eligible cases and controls, particularly the older controls. However, it is unlikely that the potential study subjects' decision to participate was affected by their dietary intake history. In addition, although our study included more than 600 female cases and 700 sex-matched controls, the statistical power to investigate the relation by NHL subtype was still limited, especially for exposures with low frequencies in the study population. Given that numerous comparisons were made in this study in assessing the association between diet and nutrient intakes and NHL risk, chance could explain some of the observed associations.

In summary, in this population-based case-control study, we found an increased risk of NHL associated with higher consumption of animal protein, saturated fat, retinol, eggs, and dairy products. We also found a significantly reduced risk associated with higher consumption of dietary fiber, tomatoes, broccoli, squash, cabbage, cauliflower, onions, leeks, mixed lettuce salad with carrots and tomatoes, and citrus fruits. Considering how little is known about the etiology of NHL, a disease rapidly increasing worldwide, further investigation of the role of dietary intakes on the risk of NHL, particularly by NHL subtype, is warranted.

TABLE 6. Food items associated with a significantly or borderline significantly† reduced risk of NHL,‡ Connecticut, 1995–2001

Food item	Cases (no.)	Controls (no.)	OR‡,§	95% CI
Fruits and vegetables				
Oranges, grapefruit, or tangerines				
<1 per month	116	113	1.0	
1–3 per month	168	202	0.8	0.6, 1.1
1–2 per week	170	244	0.7	0.5, 0.9
>2 per week	140	152	0.9	0.6, 1.2
Apples, pears				
<1 per month	83	79	1.0	
1–3 per month	167	200	0.8	0.5, 1.1
1–2 per week	169	228	0.7	0.5, 1.0
>2 per week	175	204	0.7	0.5, 1.1
Tomatoes cooked/tomato sauce				
<1 per month	156	81	1.0	
1–3 per month	160	186	0.5	0.3, 0.6
1 per week	127	229	0.3	0.2, 0.4
>1 per week	151	215	0.3	0.2, 0.5*
Broccoli				
<1 per month	77	56	1.0	
1–3 per month	184	254	0.5	0.3, 0.8
1 per week	161	192	0.6	0.4, 0.9
>1 per week	172	209	0.6	0.4, 0.9
Squash				
<1 per month	129	103	1.0	
1 per month	88	153	0.5	0.3, 0.7
2–3 per month	147	182	0.6	0.4, 0.9
>3 per month	230	273	0.6	0.5, 0.9
Cabbage/sauerkraut/ brussels sprouts				
<1 per month	302	302	1.0	
1 per month	149	231	0.6	0.5, 0.8
2–3 per month	84	100	0.8	0.6, 1.1
>3 per month	56	78	0.6	0.4, 0.9
Cauliflower				
<1 per month	281	264	1.0	
1 per month	145	182	0.7	0.6, 1.0
2–3 per month	98	168	0.5	0.4, 0.7
>3 per month	70	97	0.6	0.4, 0.9*
Onions/leeks				
<1 per month	59	51	1.0	
1–4 per month	170	192	0.7	0.5, 1.1
2–4 per week	209	252	0.7	0.4, 1.0
>4 per week	156	216	0.5	0.3, 0.8*
Mixed lettuce salad with vegetables				
<1 per month	56	44	1.0	
1–4 per month	163	167	0.8	0.5, 1.2
2–4 per week	256	333	0.6	0.4, 0.9
>4 per week	119	167	0.5	0.3, 0.8*
Salad dressing (e.g., Italian, Thousand Island, French)				
<1 per month	57	52	1.0	
1–4 per month	154	164	0.8	0.5, 1.3
2–4 per week	231	316	0.6	0.4, 0.9
>4 per week	152	179	0.7	0.4, 1.1*
Meat, fish, main dishes, lunch items				
Tuna/tuna salad/tuna casserole				
<1 per month	121	112	1.0	
1 per month	113	139	0.7	0.5, 1.1
2–3 per month	173	186	0.8	0.6, 1.1
>3 per month	187	274	0.5	0.4, 0.8*
Breads, snacks, spreads				
Dark breads				
<1 per month	116	103	1.0	
1–4 per month	131	143	0.8	0.6, 1.2
2–4 per week	209	258	0.7	0.5, 1.0
>4 per week	138	207	0.6	0.4, 0.8*
Corn bread, corn muffins				
<1 per month	386	436	1.0	
1 per month	121	157	0.8	0.6, 1.1
2–3 per month	48	75	0.7	0.4, 1.0
>3 per month	39	43	0.9	0.6, 1.4
Tortillas, all types				
<1 per month	493	546	1.0	
1 per month	64	81	0.9	0.6, 1.2
2–3 per month	21	46	0.5	0.3, 0.8
>3 per month	16	38	0.4	0.2, 0.8*
Snack chips (e.g., potato chips, corn chips, cheese crackers)				
<1 per month	237	262	1.0	
1 per month	111	98	1.2	0.9, 1.7
2–3 per month	94	125	0.8	0.6, 1.1
>3 per month	152	226	0.7	0.5, 0.9*
Popcorn				
<1 per month	314	303	1.0	
1 per month	104	141	0.7	0.5, 1.0
2–3 per month	89	128	0.6	0.5, 0.9
>3 per month	87	139	0.5	0.4, 0.8*
Mayonnaise/mayonnaise-type spreads on sandwiches/salads				
<1 per month	104	116	1.0	
1–3 per month	141	154	1.0	0.7, 1.4
1–2 per week	208	247	0.8	0.6, 1.1
>2 per week	141	194	0.6	0.4, 0.9*

Table continues

TABLE 6. Continued

Food item	Cases (no.)	Controls (no.)	OR§	95% CI
Breakfast foods and sweets				
Bacon				
<1 per month	339	364	1.0	
1 per month	99	135	0.8	0.6, 1.0
2–3 per month	79	110	0.7	0.5, 1.0
>3 per month	77	102	0.7	0.5, 1.0*
Low-fat frozen desserts (e.g., frozen yogurt/ sherbet/ice milk)				
<1 per month	366	402	1.0	
1 per month	71	94	0.8	0.6, 1.1
2–3 per month	70	85	0.9	0.6, 1.2
>3 per month	87	130	0.7	0.5, 0.9*

* p for trend < 0.05.

† Upper 95% confidence interval (CI) ≤1.0.

‡ NHL, non-Hodgkin's lymphoma; OR, odds ratio.

§ Adjusted for age, body mass index (weight (kg)/height (m)^2: <22, 22–24.5, 24.6–28, >28), family history of NHL in first-degree relatives, and total energy intake (<1,269, 1,269–1,595, 1,596–1,947, >1,947 kcal).

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TABLE 7. Food items associated with a significantly or borderline significantly† increased risk of NHL,‡ Connecticut, 1995–2001

Food item	Cases	Controls	OR‡,§	95% CI
Eggs and dairy products				
Eggs				
<1 per month	94	143	1.0	
1–3 per month	182	237	1.1	0.8, 1.6
1 per week	110	129	1.2	0.9, 1.8
>1 per week	208	202	1.4	1.0, 2.0
Milk/beverage with milk				
<1 per month	209	284	1.0	
≤4 per week	162	185	1.1	0.9, 1.5
5–7 per week	145	182	1.0	0.7, 1.3
>1 per day	78	60	1.6	1.0, 2.3
Butter or margarine on bread				
<1 per month	80	137	1.0	
1–4 per month	94	121	1.3	0.9, 1.9
2–4 per week	193	235	1.3	0.9, 1.8
>4 per week	227	218	1.6	1.1, 2.3*
Cream soups (e.g., chowders, potato soup)				
<1 per month	354	436	1.0	
1 per month	120	161	0.9	0.7, 1.1
2–3 per month	71	80	1.0	0.7, 1.5
>3 per month	49	34	1.6	1.0, 2.5
Ice cream, milkshake				
<1 per month	85	239	1.0	
1 per month	89	143	0.8	0.6, 1.1
2–4 per month	174	221	1.0	0.7, 1.3
>4 per month	146	108	1.5	1.1, 2.1*
Fruits and vegetables				
Lettuce, plain lettuce salad				
<1 per month	298	382	1.0	
1–4 per month	127	146	1.2	0.9, 1.5
2–4 per week	124	116	1.4	1.0, 1.8
>4 per week	45	67	0.9	0.6, 1.3
Cooked greens (e.g., spinach, mustard greens, turnip greens)				
<1 per month	192	229	1.0	
1 per month	104	154	0.8	0.6, 1.1
2–3 per week	137	122	1.3	1.0, 1.8
>2 per week	161	206	0.9	0.7, 1.2
Sweet potatoes, yams				
<1 per month	234	330	1.0	
1 per month	141	164	1.2	0.9, 1.5
2–3 per month	114	99	1.6	1.2, 2.2
>3 per month	105	118	1.2	0.9, 1.6
Meat, fish, main dishes, lunch items				
Spaghetti/pasta with meat sauce				
<1 per month	123	191	1.0	
1 per month	129	141	1.4	1.0, 1.9
2–3 per month	170	176	1.4	1.0, 1.9
>3 per month	172	203	1.2	0.8, 1.6
Breads, snacks, spreads, sweets, and breakfast foods				
White bread				
<1 per month	100	137	1.0	
1–4 per month	112	179	0.9	0.6, 1.3
2–4 per week	187	221	1.1	0.8, 1.6
>4 per week	195	174	1.5	1.0, 2.0*
Cereal, cold or cooked				
<1 per month	70	108	1.0	
1–4 per month	121	152	1.2	0.8, 1.8
2–4 per week	200	203	1.4	1.0, 2.1
>4 per week	203	248	1.2	0.8, 1.7

Table continues

TABLE 7. Continued

* p for trend < 0.05.

† Lower 95% confidence interval (CI) ≥1.0.

‡ NHL, non-Hodgkin's lymphoma; OR, odds ratio.

§ Adjusted for age, body mass index (weight (kg)/height (m)^2: <22, 22–24.5, 24.6–28, >28), family history of NHL in first-degree relatives, and total energy intake (<1,269, 1,269–1,595, 1,596–1,947, >1,947 kcal).

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